



UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/284,683	06/24/1999	GREGOR CEVC	35946-701.831	2670

21971 7590 11/25/2008
WILSON SONSINI GOODRICH & ROSATI
650 PAGE MILL ROAD
PALO ALTO, CA 94304-1050

EXAMINER

KISHORE, GOLLAMUDI S

ART UNIT	PAPER NUMBER
----------	--------------

1612

MAIL DATE	DELIVERY MODE
-----------	---------------

11/25/2008

PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No. 09/284,683	Applicant(s) CEVC, GREGOR	
	Examiner Gollamudi S. Kishore, Ph.D	Art Unit 1612	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 18 August 2008.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 106-110, 112-115, 118 and 120-138 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 106-110, 112-115, 118 and 120-138 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
 2. ☐ Certified copies of the priority documents have been received in Application No. _____.
 3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|--|---|
| 1) <input type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413) |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | Paper No(s)/Mail Date. _____ |
| 3) <input checked="" type="checkbox"/> Information Disclosure Statement(s) (PTO/SB/08) | 5) <input type="checkbox"/> Notice of Informal Patent Application |
| Paper No(s)/Mail Date <u>8-18-08, 12-26-07</u> . | 6) <input type="checkbox"/> Other: _____ |

DETAILED ACTION

The RCE dated 8-18-08 is acknowledged.

Claims included in the prosecution are 106-110, 112-115, 118 and 120-138.

Claim Rejections - 35 USC § 112

1. The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

2. Claims 106-110, 112-118 and 120-138 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. Instant claims recite 'consisting essentially of' with further limitations of 'salt of one ore more non-steroidal anti-inflammatory drugs'. A careful review of the specification indicates that when only phosphatidylcholine is used in the formation of a vesicle, applicant uses NSAID as such and not a salt (Examples 8-17 with PC and diclofenac; Examples 18-25 with PC and ibuprofen). Rest of the examples use a surfactant in addition. Thus the combination of 'consisting essentially of' as applied to salts of NSAIDs is deemed to be new matter.

Claim

Rejections -

35 U.S.C. §

103

3. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

4. Claims 106-110, 112-118 and 120-138 are rejected under 35 U.S.C. 103(a) as being unpatentable over Vyas (Journal o micro encapsulation, 1995) or Hayward (5,585,109) or Sheffield (4,937,254) in combination r Radhakrishnan (5,043,165), Edger (5,498,420) by themselves or together in further combination with Mezei (4,897,269).

Vyas discloses topical application of liposomes consisting essentially of PC and diclofenac in PBS, pH 7.4 (abstract, Table 1 formulation L1).

Hayward discloses liposomal formulations containing soy lecithin and salicylic acid and a method of delivery to the skin. The carrier material is polymethacrylate gel. The pH is 6.5 to 7.5. The composition further contains antioxidants and preservatives and hydrocolloids (columns 3-7). What is lacking in Hayward is the use of claimed antioxidants and Stabilizers.

Art Unit: 1612

Sheffield teaches a method of topical administration of liposomal formulations containing phosphatidylcholine and NSAID. The method of administration is topically and either internally or externally which implies skin. The composition further contains PBS and hydrocolloids (col. 3, lines 7-56; col. 6, line 15 through col. 7, line 12, Examples 13-15).

What is lacking in Vyas, Hayward or Sheffield is the inclusion of benzyl alcohol. Vyas and Sheffield also do not teach the use of unilamellar vesicles of instant sizes. Hayward is silent with respect to the nature of the liposomes.

Radhakrishnan while disclosing liposomal formulations teaches that multilamellar preparations can be treated to produce small unilamellar vesicles, large unilamellar vesicles or oligolamellar vesicles which are characterized by sizes in the 0.04-0.08 microns, 0.1 to 0.5 microns and mixed micron range. Radhakrishnan further teaches that the advantage of the suvs is the greater packing density of the liposomes at a mucosal surface and suvs are preferred for topical or nasal use (col. 7, line 45 through col. 8, line 14).

Edger while disclosing liposomal formulations for topical use teaches that from statistical point of view the interaction of small unilamellar vesicles with other cells is likely to be greater than that of multilamellar vesicles which facilitates the transfer of membrane constituents (col. 1, line 48 through col. 2, line 10).

Mezei while disclosing liposomal compositions teaches the addition of preservatives and antioxidants such as benzyl alcohol and tocopherol (abstract, Example 4 and col. 14, lines 42-63).

Art Unit: 1612

The use of small unilamellar vesicles of claimed sizes would have been obvious to one of ordinary skill in the art because of the advantages taught by Radhakrishnan and Edger. The addition of antioxidants and stabilizers in the compositions of Vyas or Hayward or Sheffield would have been obvious to one of ordinary skill in the art since such an addition would prevent oxidation of lipids and degradation by bacteria respectively as taught by Mezei. What is lacking in Hayward is the teaching of the use of synthetic phospholipid. However, since liposomes can be formed with either natural or synthetic phospholipids, it is deemed obvious to one of ordinary skill in the art to choose the desired source with a reasonable expectation of success. Hayward and Sheffield also lack the teaching of the application of the claimed amount of the liposomes on the skin surface. However, since the amount applied depends upon the condition to be treated and the severity of the condition, it is deemed obvious to one of ordinary skill in the art to manipulate this parameter to obtain the best possible results.

Applicant's arguments have been fully considered, but are not found to be persuasive. Applicant argues that Vyas does not teach or suggest recited vesicles. This argument is not persuasive since Vyas teaches liposomes consisting essentially of PC and diclofenac. With regard to instant limitation of permeability factor between 2 and 4, the examiner points out that Radhakrishnan teaches the advantage of suvs is the greater packing density of the liposomes at a mucosal surface and suvs are preferred for topical or nasal use; instant claims recites mucosal membranes. Edger also teaches the advantages of smaller vesicles. With regard to antioxidants, Mezei teaches both benzyl alcohol and tocopherol. Applicant's arguments that Vyas teaches away since he

Art Unit: 1612

shows that vesicles having a mixture of PC and either dicetyl phosphate or cholesterol when loaded with diclofenac, release approximately 1.7 to 3 times more diclofenac than vesicles having phosphatidyl choline alone are not persuasive since instant claims do not recite any 'release amounts'.

Applicant argues that Sheffield does not teach or suggest a vesicle that is capable of penetrating through a permeability barrier having at least one constriction, wherein the vesicle is larger than the constriction by more than a factor of 2 and less than a factor of 4. These arguments are not persuasive since the rejection is made on the combination of references which include Radhakrishnan and Edger and the examiner has already addressed those arguments. The examiner has already addressed applicant's arguments of Hayward's teaching away from the use of salts of NSAIDs in the previous action. In response to the examiner's position, applicant argues that pKa of most NSAIDs is between 3 and 5 as evident from Bosck et al, and based on the Henderson-Hasselback equation, an NSAID whose pKa=5 will be present in at least some salt form, if not predominantly in the salt form even at pH 3. This argument is not persuasive since 'most of NSAIDs' does not mean all of the NSAIDs behave the same way and all of them are weak acids. The reference submitted does not say anything about salicylic acid taught by Hayward. Furthermore, as applicants themselves previously stated that instant composition contains even NSAID not in a salt form.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Gollamudi S. Kishore, Ph.D whose telephone number is

Art Unit: 1612

(571) 272-0598. The examiner can normally be reached on 6:30 AM- 4 PM, alternate Friday off.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Krass Frederick can be reached on (571) 272-0580. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Gollamudi S Kishore/
Primary Examiner, Art Unit 1612

GSK